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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/825,155	04/03/2001	Ariel Ruiz i Altaba	1049-1-008 N CON	2618

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EXAMINER	
NICKOL, GARY B	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/825,155	ALTABA, ARIEL RUIZ I	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) *1-8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Corrected Filing receipt

Response to Amendment

Re: Altaba, A.

Date of priority: June 20, 1997

The Amendment filed January 16, 2004 in response to the Office Action of October 15, 2003 is acknowledged and has been entered.

Claims 1-9 are pending.

Claims 1-8 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

Claim 9 is currently under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Inventorship

In view of the papers filed 01/16/04, it has been found that this nonprovisional application, as filed, through error and without deceptive intent, improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 CFR 1.48(a). The inventorship of this application has been changed by the addition of Nadia Dahmane as co-inventor.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of the file jacket and PTO PALM data to reflect the inventorship as corrected.

Drawings

The replacement drawing was received on 01/16/04. This drawing is acceptable.

Rejections Maintained:

Claim 9 remains rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to *enable* one skilled in the art to which it pertains, or with which it is most nearly connected, to predictably use the invention as claimed for the reasons of record (see Actions mailed 10/15/2003 & 11/12/2002).

Applicants argue (pages 5-6) that the data supplied with the declaration is commensurate in scope with the teaching of the specification (particularly on pages 2-3, and 10). Applicants further argue that they have provided evidence as to the role of Gli1 expression in basal cell carcinoma (BCC). Applicants further argue that because there is a strong correlation between the cellular dysplasia, tumor formation and the presence of Gli1 in tumor cells, it is "likely" that agents that inhibit the expression and or function of Gli1 are "probable" candidates as inhibitors of cellular proliferation and tumor growth and would be effective when delivered as a pharmaceutical composition. These arguments have been carefully considered but are not found

persuasive. As set forth in the Action mailed 10/15/2003, there is no guidance for one of skill in the art to predictably choose and use siRNA's in a pharmaceutical composition. Moreover, the disclosure fails to teach any particular structure or composition that would predictably function as a pharmaceutical composition for the intended purpose of treating a cellular debilitation, dysfunction, and or other disease state in mammals caused by the development and presence of sporadic basal cell carcinoma. Applicants are reminded that the specification must contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to, to make and use the same (first paragraph of 35 U.S.C. 112). Thus, the assertion that certain agents may *potentially* inhibit the expression and or activity of Gli1 fails to provide sufficient guidance and objective evidence to one skilled in the art to predictably and successfully *use* a pharmaceutical composition comprising a therapeutically effective amount of inhibitors of Gli1 for the intended purpose of treating disease states in mammals caused by the development and presence of sporadic basal cell carcinoma.

Applicants further appear to substantiate the Office's position that the data supplied with the declaration was *not* commensurate in scope with the teaching of the specification because applicants admit that the specification does not directly disclose the specific inhibitors (siRNA molecules) provided for in the declaration (bottom of page 6, & page 7, 2nd paragraph, lines 3-4- applicants admit siRNAs were not claimed). Hence, arguments directed at reiterating the results presented in the declaration (top of page 7) are not found persuasive since said declaration was previously considered. Applicants further remark that they have amended claim 9 to include anti-sense molecules and antibodies as antagonists of Gli1. Applicants further note that they have provided additional positive data to support the inclusion of these agents into pharmaceutical

composition claims wherein the additional data may be found in an article published by in the inventor attached as Appendix A. This argument has been considered but is not found persuasive because there appears to be no such article or appendix (only Appendix B and C appear to have been included) that was submitted with applicant's response. Further, applicants do not mention whether or not the anti-tumor activity reported was displayed in-vitro or in-vivo. As set forth previously, the greatly increased complexity of the in vivo environment as compared to the very narrowly defined and controlled conditions of an in- vitro assay does not permit a single extrapolation of in vitro assays to human diagnostic efficacy with any reasonable degree of predictability. Applicants further argue (page 7) that information provided in Appendix B (Vickers *et al.*) supports the reconsideration of the previously submitted declaration drawn to siRNA molecules because the article teaches that siRNA molecules appear to have similar mechanistic properties as antisense RNAs. This argument has been considered but is not found persuasive. The Vickers *et al.* article was published in 2002, and there is no evidence to suggest (either with antisense or siRNA) that the claims are enabled at the time of filing. Applicants further provide Appendix C related to the use of antisense molecules under study in clinical trials, with the information provided having a publication date of 1994. This argument has been considered but is not found persuasive as the antisense used in the clinical trials is not specific nor related to the inhibition of the expression of Gli1. Thus, applicant's arguments have not been found persuasive and the rejection is maintained.

Claim 9 remains rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not *described* in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons of record (Action mailed 10/15/2003).

Applicants do not appear to have specifically addressed the written description rejection with regards to the claimed invention. While it is noted that applicant's have amended the claims to include "antisense RNA molecules" and "antibodies to Gli1", there is no description of the structure of these molecules and or a description of the structure of small molecule antagonists of Gli1 expression and activity, or ligands of Gli1 or agents that exhibit mimicry to Gli1 or antagonism to Gli1 or control over the production of Gli1. Thus, it remains that the specification fails to provide sufficient guidance and or a description of molecules and or structures encompassed by the broad genus of inhibitors intended as pharmaceutical compositions. Thus, applicant's arguments have not been found persuasive and the rejection is maintained.

No claim is allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

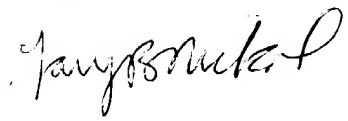
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 571-272-0835. The examiner can normally be reached on M-Th, 8:30-5:30; alternate Fri., 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary B. Nickol Ph.D.
Primary Examiner
Art Unit 1642

GBN



GARY NICKOL
PRIMARY EXAMINER